Heliobacter pylori – within and beyond the digestive tract (European Heliobacter pylori Study Group)

S106 Epidemiology of Helicobacter pylori infection. A worldwide perspective

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Helicobacter pylori infection constitutes the most common chronic bacterial infection worldwide. In developing countries, most of the population is infected and acquisition of the infection occurs in early childhood, while in developed countries the rate of infection is positively correlated with increasing age, explained by an observation which related to the existence of a cohort effect. Despite its high prevalence, *H. pylori* is not a commensal or saprophytic bacterium. In contrast to other Helicobacters, present in animal stomachs, *H. pylori*, the Helicobacter adapted to humans, constantly induces inflammation and lays the groundwork for most of the major diseases of the stomach, including peptic ulcer and gastric cancer. Measures to prevent the transmission of this bacterium cannot be taken because the mode of transmission is not known. Despite a colony of laboratory cats found to be infected, humans are considered the only source of infection. In developing countries transmission via water and food is plausible. Contaminated water has been found, but only detected by PCR. Experimentally, flies exposed to *H. pylori* cultures can transport the bacteria. However, in developed countries direct person-to-person transmission is most likely, especially within families. Molecular fingerprinting has shown that transmission occurs probably between spouses and their children. Another potential hazard is linked to contact with gastric juice in the line of one's profession. The wide distribution of the infection makes is a public health problem.

S107 *Helicobacter pylori* – Within and Beyond the Digestive Tract

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Colonisation of the foregut by *Helicobacter pylori* (Hp) is now believed to be one of the commonest chronic infections in the human. Hp infection, usually acquired in childhood, profoundly affects gastric function, producing either increased (predominantly antral gastritis), or decreased (predominantly corpus gastritis) gastric acid secretion. Factors determining the differential response to Hp infection are incompletely understood. The bacterium exhibits marked polymorphism and toxic strains are increasingly characterised. Hp antritis is associated with increased risk of duodenal ulcer, Hp corpusitis with increased risk of gastric cancer. MALT lymphoma is also associated with Hp infection and may remit on eradication of the organism. However, most infected subjects develop superficial chronic gastritis with no significant clinical consequences. The diagnosis and treatment of Hp infection has become very effective. Bacterial resistance to metronidazole or clarithromycin is an important and increasing problem. It has been suggested that conditions outside the alimentary tract may be associated with Hp infection, but the evidence for this is incomplete. These comprises short stature, coronary heart disease, among others.

S108 The Role of H pylori in the Pathogenesis of Gastric MALT Lymphoma

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That lymphoma should arise from gastric mucosa is paradoxical since there is no lymphoid tissue in the normal stomach. Lymphoid tissue with the characteristics of MALT accumulates in gastric mucosa almost exclusively as a consequence of H pylori infection. The clinical, histological and molecular genetic properties of low grade gastric MALT lymphoma suggest that its growth is influenced by a local antigen. Evidence for a link between H pylori and gastric lymphoma is the finding of H pylori in over 90% of cases of gastric MALT lymphoma, the higher incidence of gastric lymphoma in communities with a high prevalence of H pylori and a case control study showing that gastric lymphoma is commoner in patients with a history of infection with the organism. Laboratory studies have shown that the growth of tumour cells from low grade gastric lymphomas can be stimulated by H pylori and that the effect is strain specific and mediated by H pylori specific T-cells. Parallel clinical studies have shown that cases of low grade gastric lymphoma, when confined to the mucosa, may regress following eradication of H pylori from the patient's stomach and that relapse of the infection may lead to recurrence of lymphoma.

S109 Extra-Gastrointestinal Manifestations of *Helicobacter pylori* Infection

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The dirty chicken hypothesis (Solomans 1993) is based on the observation that chickens bred in overcrowded unhygienic conditions do not grow well. If these chickens are given antibiotics, their growth improves. It was postulated that a low grade systemic acute phase response may be responsible. We have postulated that *H. pylori* infection may be producing a dirty chicken effect in man. It is associated with a low grade acute phase response, and the main risk factors for transmission are poor hygiene and overcrowding. It is also associated with diminished growth in childhood and cardiovascular disease in adult life. The evidence is generally supportive of a moderate effect, although confounding by social and economic factors cannot be ruled out. Most cardiovascular risk factors are actually acute phase reactants. We are now carrying out interventional studies to check the effect of appropriate antibiotics on cardio risk factors and on mortality.

S110 Strategies in Vaccine Development

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The high incidence of *H. pylori* infection worldwide, its potential complications and the rapid emergence of antibiotic resistance demand the development of novel measures of disease control, including vaccines. The feasability of latter approach was first supported by the demonstration that mice immunized orally with a lysate of *Helicobacter felis*, a bacterium closely related to *H. pylori*, were protected against subsequent challenge. Because of the poor characterization of bacterial lysates and their greater potential for side effects, the focus of vaccine development has shifted to the identification of protective antigens to be used as subunit vaccines with an adjuvant or to be expressed in live vaccine vectors. Several antigens of *H. pylori* are now considered vaccine candidates, including urease, VacA, and two heat shock proteins, HspB and HspA. Furthermore, we and others demonstrated that therapeutic immunization was possible against an established infection, opening the possibility to use vaccination as

a therapy. Protection and cure have been associated with increased antigen-specific T_H2 cell responses. The role of secretory IgA and/or of IgG in the protection of the gastric mucosa remains however unclear. We also showed that oral immunization with urease was safe in *H. pylori*-infected humans and could reduce the density of infection. Further developments include the use less toxic adjuvants or of live vaccine vectors, the determination of the optimal immunization procedure to induce protection of the gastric mucosa as well asthe use of combinations of antigens.

The Carbapenem Decade

S111 Comparative Evaluation of Carbapenems in Intra-Abdominal Infections

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Objectives: Imipenem/cilastatin (I/C) has been shown to be highly effective as monotherapy in the treatment of intra-abdominal infections. Meropenem (Me), a carbapenem with an I/C like spectrum of activity, has been reported in two recent clinical trials (in one I/C 3 gr vs Me 3 gr day and in the other I/C 1.5 gr vs Me 1.5 gr day) to have as good a safety and efficacy profile as I/C. The aim of this paper is to compare the results obtained in the three trials.

Methods: We undertook an open label, prospective, randomized, parallel multicenter study to compare the efficacy and tolerability of 1.5 gr of I/C with 3 gr of Me day. These dosages were chosen because: 1 Me is recommended at 3 gr/day in intra-abdominal infections while I/C is effective at 1.5 gr, 2 I/C has greater activity on Enterococcus (four times higher). Of 287 patients enrolled in 20 centers, 201 patients were evaluable (101 randomized to I/C and 100 to Me). In the 86 (31.8%) non evaluable patients 94.1% were excluded owing to failure to recover susceptible pathogens. Comparative analysis shows that our patients were more severe than those in the other studies: fewer cases of appendicitis (15% vs 35% and 73%) and more cases in the moderate severe group according to APACHE II score.

Results: Although the clinical and bacteriological outcome were not significantly different, at the start of our study with I/C, 9 pathogens sensitive to I/C were resistant to Me and of the 15 Enterococcus sp. sensitive to I/C 6 were resistant to Me. Furthermore, in our study both the mean time to defervescence (1.83 days vs 2.46 days $p = 0.046$) and the average duration of therapy (6.7 days vs 4.2 days = 0.019) were significantly shorter in the I/C group. Seizures did not occur in any of the trials even when 1 gr/8 hr of I/C was employed.

Conclusions: The fact that I/C was clinically efficacious at half the dosage of Me and required a shorter duration of treatment, even though the patients treated with I/C appeared to be more severe that those in the Me group clearly suggests that I/C is significantly more cost effective, at least with respect to the cost of the antibiotic itself.

S112 Extended-Spectrum Beta-lactamases: Epidemiology and Clinical Implications

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Gram negative pathogens harboring extended-spectrum beta-lactamases (ESBLs) are becoming an increasing therapeutic problem globally. We have recently published an analysis of an in-vitro resistance survey among 33,869 gram negative organisms from 396 intensive care units in the United States. The prevalence of ceftazidime-resistance among *Klebsiella* isolates in this survey rose from 3.6% to 14.4% between 1990 and 1993 (Itokazu. *Clin Infect Dis* 1996; 23: 779).

A molecular epidemiologic investigation of an epidemic of 31 bloodstream infections with multi-resistant *Klebsiella* and *E. coli* in a university hospital in Chicago revealed that most cases occurred in debilitated nursing home (NH) patients who were instrumented, had high APACHE scores, and had recently been treated with antibiotics, especially extended-spectrum cephalosporins (ESCs). In this outbreak and in a similar epidemic reported in 1993 from a hospital in New York City, patients treated with imipenem and/or amikacin had a higher survival rate than those treated with ESCs (Schiappa. *J Infect Dis* 1996; 174: 529).

We are currently investigating a city wide outbreak of ESBL-producing pathogens among NH patients admitted to 6 Chicago hospitals mediated by a common 54 Kb plasmid. Prior exposure to oral TMP-SMX and/or quinolones was a risk factor for colonization with an ESBL-producer in this study.

S113 Reduction of Cyclosporin Nephrotoxicity in Transplant Patients

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No abstract available.

S114 The Economics of a New Delivery System

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Objectives: to explain the differencies between the different preparation methods of IV drugs.

Methodology: the conventional methods, i.e. syringe-needle and transfert needle were compared with the Monovial ®, a drug container with an integrated transfer system. In a first step all relevant costs of each method were established and the cost of each activity was calculated. In a third step these global costs were calculated for a sample of 10 drugs commonly used in the hospital. Finally the opinion of 31 nurses was examined by means of two open and 9 score statements.

Results: the transfer-needle method was the most expensive way to prepare drugs for IV administration (31.73 BEF) followed by the syringe-needle method (23.23 BEF). Monovial ® is the cheapest method for the preparation of IV drug administration (10.71 BEF). In the general opinion of the nurses, the preparation of IV drugs by means of the Monovial ® is an improvement in terms of speed, ease of use and reduces of the amount of waste, safety and asepsy.

Conclusion: new administration devices can diminish preparation time.

S115 Microbiological Overview of the Carbapenems

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The carbapenems are formidable antimicrobials, with broader spectra than any other β-lactam. Of the compounds available, imipenem has been widely used for 12 years and meropenem for 2; panipenem is used in Japan, not elsewhere. Meropenem is the most active against gram-negative bacteria, imipenem the most active against against gram-positive cocci. All retain activity against AmpC-derepressed enterobacteria and those with ESBLs. To date, *P.*